

Participants/materials, setting, methods: RPL patients completed an online questionnaire before first consultation at the Danish RPL clinic. Eligible controls were retrieved from the Internet based cohort study 'snartforældre.dk'. Cohen's Perceived Stress Scale was used to assess self-reported stress and the Major Depression Index assessed symptoms of depression. Comparisons were made by Chi² testing.

Main results and the role of chance: We invited 438 women with RPL to participate in the study and 292 (67%) completed the questionnaire. Of these, 25 (9%) had symptoms corresponding to the ICD-10 diagnosis of "moderate-severe depression" - in DSM-IV terms "major depression". A high stress level, defined as a score of >16 on the perceived stress scale, was reported by 153 (52%) patients.

Among controls, 46 (2%) had symptoms of major depression and 675 (34%) had high stress levels. The differences between patients and controls were highly significant for both stress and depression, $p < 0.0001$ in both cases.

Limitations, reason for caution: There may be a bias in who chooses to complete both the patient questionnaire and the online survey. Furthermore, no information was available whether any of the women in the comparison group actually had RPL, but the diagnosis is seen in <1% of women in the background population.

Wider implications of the findings: We have shown that symptoms of stress and major depression are significantly more prevalent among women referred for RPL than among women without known fertility problems. Both stress and major depression have high personal and socio-economic costs and therefore need to be considered in the management of this patient group. How stress and depression and their treatment impact pregnancy prognosis are to be investigated in future studies.

Study funding/competing interest(s): Funding by University(ies), University of Copenhagen has given a PhD grant to A.M. Kolte. No specific funding was sought for this study.

Trial registration number: N/A.

O-081 Increased risk of intimate partner violence associated with infertility or subfertility: a systematic review

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Study question: The purpose of this systematic review was to assess the available evidence on the effect that a diagnosis of infertility or an inability to become pregnant (subfertility) in women of reproductive age results in an increased risk for experiencing intimate partner violence (IPV).

Summary answer: The diagnosis of infertility/presentation of subfertility have been identified as a risk factor for intimate partner violence in specific settings and countries. The potential drivers for risk of intimate partner violence associated with this disease/disability appear to be distinct from other forms of violence against women.

What is known already: A United Nations report on global and regional estimates of violence against women, documented "not only how widespread this problem is, but also how deeply women's health is affected when they experience violence." Consequences of violence against women can result in serious injury and death, as well as emotional, verbal, psychological, and economic negative outcomes. Additionally, having fewer children than desired or expected is not only a medical concern but a socially constructed problem.

Study design, size, duration: A systematic review of literature following PRISMA guidelines was completed on articles published between and inclusive of years 2000 and 2013. Multiple preliminary searches prior to 2000 did not identify quantitative studies meeting the criteria. Seven electronic global databases and experts were contacted and criteria applied independently by two investigators.

Participants/materials, setting, methods: Studies were searched /assessed to address the following question: The effect that a diagnosis of infertility or subfertility (intervention exposure) in comparison to those without a fertility problem (comparator) women of reproductive age (population) that results in an increased risk for experiencing intimate partner violence (IPV) - outcome.

Main results and the role of chance: Out of 409 studies initially identified, 314 abstracts and 63 articles were assessed. Eighteen studies analysing the relationship between infertility/subfertility (as the exposure) and intimate partner violence (as the outcome) in a quantitative manner met the final inclusion criteria, however, qualitative studies mentioning a correlation without providing quantitative data were excluded, as were three studies which investigated the

outcome indicator and exposure in the reverse. All of the studies evaluated various forms of violence against women, including physical and sexual violence. Ten studies indicate that the infertility/subfertility is a risk factor for intimate partner violence; and three high-quality studies find a significant correlation between the exposure and outcomes of physical and sexual violence.

Limitations, reason for caution: Terminology for both infertility/subfertility; Terminology describing violence against women; Few quantitative prospective studies identified; Most studies cross-sectional; and, "Selection bias" from fertility clinic-based versus poor capture in population-based studies, all present limitations/caution. Proving causality of infertility/subfertility as a definitive risk factor and lack of direct comparisons between studies present limitations.

Wider implications of the findings: Gender-based violence is inextricably linked to women's lower status in many societies as compared to men. In these same settings, Infertility/subfertility can often be inappropriately assigned as fault of the woman, since fertility manifests itself through pregnancy. Assessment tools addressing risk of harm are needed when diagnosis of infertility/subfertility occurs within settings identified through this review. Quantitative prospective studies are needed in diverse global settings, in order to assess differing effects of male/female infertility/subfertility diagnosis.

Study funding/competing interest(s): Funding by national/international organization(s), Unspecified core funds from HRP: The UNDP, UNICEF, UNFPA, WHO and World Bank Special Programme of Research, Development and Research Training in Human Reproduction.

Trial registration number: Not applicable.

O-082 Male psychological adaptation to infertility: a systematic review of longitudinal studies

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Study question: What are the psychological symptoms associated with the experience of infertility in men, how do they vary over time, and which act as risk or protective factors?

Summary answer: The psychological well-being of men facing infertility seems to deteriorate significantly 1 year after the first fertility appointment. This review identified three predominant risk factors for psychological maladjustment - active-avoidance coping, catastrophizing and difficulty in partner communication - and one main protective factor - the use of meaning-based coping strategies.

What is known already: Biological, cultural and social aspects differentiate the medical and psychological circumstances related to the experience of infertility between men and women. Previous studies have suggested that facing infertility might be in its essence a different experience for men and women. Even though there is vast evidence on the emotional adjustment of women to infertility, there are no systematic reviews focusing on the male psychological adaptation to infertility.

Study design, size, duration: A systematic review aiming to identify studies on male psychological adaptation to infertility was performed by conducting a literature search from inception to August 2013 on ISI Web of Science, Medline, PsycArticles, Scielo and Scopus. Guidelines of Cochrane Collaboration and Preferred Reporting Items were followed.

Participants/materials, setting, methods: A search was conducted using combinations of MeSH terms (e.g. 'male, infertility') and keywords (e.g. 'emotional adjustment'; 'distress'; 'depression'). Studies in English, French and Spanish were considered, and had to present longitudinal data to be eligible. A narrative synthesis approach was used to conduct the review.

Main results and the role of chance: Ten studies from 3 continents were eligible from 1435 records identified in the search. Results revealed that psychological symptoms of maladjustment significantly increased in men 1 year after the first fertility appointment. Excepting for the desire to have a child, which significantly decreased, no significant differences were found two or more years after the initial consult. Evidence was found for active-avoidance coping, secrecy, difficulty in partner communication, catastrophizing, importance of a biological family, unsuccessful treatments and duration of treatment as risk factors for psychological maladjustment. Using meaning-based and active-confronting coping strategies before entering treatment were

significant protective factors against distress. Active-avoidance coping was also found to be a risk factor for marital adjustment, while meaning based coping was found to be a protective factor.

Limitations, reason for caution: The number of follow-up studies testing significant differences or predictors was limited. Because most samples were from Europe and the United States, there is a high risk of cultural and demographic bias. Although these studies constitute the best available evidence, a cautious approach to data interpretation is required.

Wider implications of the findings: This is the first systematic review on male psychological adaptation to infertility overtime. Our findings suggest that counseling infertile men should include interventions with coping skills training in order to promote adaptive coping strategies to deal with the challenge of infertility. Further prospective large studies with good quality design and power are warranted to perform a subsequent meta-analysis and compare results concerning diagnosis and treatment options.

Study funding/competing interest(s): Funding by national/international organization(s). This work is supported by European Union Funds (FEDER/COMPETE - Operational Competitiveness Programme) and by national funds (FCT - Portuguese Foundation for Science and Technology) under the projects PTDC/MHC-PSC/4195/2012 and SFRH/BPD/85789/2012.

Trial registration number: N/A.

INVITED SESSION

SESSION 21: THE LATEST FINDINGS FROM THE REPROTRAIN CONSORTIA

Monday 30 June 2014

17:00 – 18:00

O-083 From mouse to human via flies; the latest interdisciplinary andrology research

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An ongoing interdisciplinary andrology research initiative in Europe is the “Reproductive Biology Early Research Training” network (Reprotrain); a UE funded project involving seven different research laboratories and two companies (www.reprotrain.eu). The overall objectives of Reprotrain are 1) to provide a comprehensive interdisciplinary training programme for early stage researchers in state-of-the-art male Reproductive Biology and Andrology, 2) to overcome historical fragmentation in the field of spermatogenesis and Andrology research by integrating and implementing different disciplines in male Reproductive Biology and Medicine, 3) to develop and implement systems biology based approaches (genomic, proteomic, transcriptomic, epigenetic and metabolomic), and 4) to develop novel clinical and industrial applications. Ten Early Stage Researchers and four Experienced Researchers are performing studies in genetics and epigenetics, molecular male reproductive medicine, molecular and structural biology, and biotechnology with hands-on training in cutting-edge technologies relevant to current molecular-genetic and medical research. The training network integrates individual research projects based on clinical samples and key selected model organisms (mouse and flies).

As an example of the development of two of the Reprotrain projects, the research lines developed on the proteomics and epigenetics of the sperm cell is presented. Previous knowledge established that the mammalian sperm cell DNA is packaged by protamines while a small fraction remains associated with nucleosomes enriched at loci of developmental importance. But the distribution of other proteins, in addition to protamines and histones, in the different sperm chromatin fractions had not yet been explored. Therefore we initiated a detailed proteomic and genomic characterization of the sperm chromatin in order to increase the epigenetic knowledge of the male germ cell and determined whether quantitative alterations in chromatin proteins were present in infertile patients. Dissected sperm chromatin fractions were subjected to shotgun protein identification using mass spectrometry and deep genome sequencing of the DNA. Our results indicate that the sperm cell chromatin delivers to the offspring a rich combination of histone variants, transcription factors, chromatin-associated and chromatin-modifying proteins

differing in chromatin affinity, which may be involved in the regulation of histone-bound paternal genes after fertilization. The differential proteomic results also suggest that alterations in the proteins involved in chromatin assembly and metabolism may originate epigenetic errors during spermatogenesis, resulting in inaccurate sperm epigenetic signatures, which could ultimately prevent embryonic development. Funded by a Marie Curie Initial Training Network (FP7-PEOPLE-2011-ITN-289880).

O-084 Is the promise of sperm transcriptomics being kept?

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Is the promise of sperm transcriptomics being kept?

Since the initial reports of transcription (RNA) in sperm appeared in the early 1960s, controversy over its purpose has existed ever since. A renewed interest in the field from the mid 1990s onward has led to many reports on the presence, characterisation and role of sperm RNA in a variety of species (including some plants). Because it can serve as a proxy for the testis, sperm transcriptomics promises to provide valuable, non-invasive insights into the health of the testis in general and individual fertility in particular. The key to wider acceptance is threefold. Firstly, there must be some clinical demonstration of the utility of sperm RNA in a truly diagnostic setting. Secondly, the diagnostic technology must be relatively inexpensive and thirdly, the technology (and its accompanying bioinformatics) must be more readily accessible (end-user friendly). To date, considerable progress with the first and second requirements has been made, but there is still some way to go before the third requirement is met. Recent publications of array-based approaches capable of identifying semen samples whose partners went on to achieve a pregnancy are very encouraging. Next generation sequencing is going to greatly improve our understanding of functional aspects of sperm RNA that will no doubt help inform the choice of a good panel of markers for a cheap diagnostic assay. Reprotrain is funding one such comparative transcriptomic study examining a range of animal species including human, bovine, porcine and ovine that seeks to define and hopefully refine the RNA profile of mammalian sperm in relation to its function, both in the spermatozoon and possibly the early embryo.

References:

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SELECTED ORAL COMMUNICATION SESSION

SESSION 22: REPRODUCTIVE SURGERY

Monday 30 June 2014

17:00 – 18:00

O-085 A multicentre randomised study of pre-IVF outpatient hysteroscopy in women with recurrent IVF-et failure – the trophy trial

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